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HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN

for

ROSINS
AND
ROSIN SALTS

CAS No. 8050-09-7
CAS No. 65997-06-o
CAS No. 68425-08-I
CAS No. 61790-50-9
CAS No. 61790-51-O
CAS No. 68783-82-4

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Submitted to the US EPA

By

The Pine Chemicals Association, Inc.
HPV Task Force
Consortium Registration

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Test Plan For Rosins and Rosin Salts

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Summary

The Pine Chemicals Association, Inc. (PCA) is sponsoring 36 HPV chemicals. This Test Plan addresses the following six chemicals, known collectively as Rosins and Rosin Salts:

CAS 8050-09-7, Rosin
CAS 65997-06-0, Rosin, hydrogenated
CAS 68425-08-1, Rosin, distillation overheads
CAS 68783-82-4, Rosin, low boiling fraction
CAS 61790-50-9, Rosin, potassium salt
CAS 61790-51-0, Rosin, sodium salt

All of the members of this group of substances are closely related to rosin, which is a naturally occurring substance found in trees, predominantly pine trees. Rosin is composed primarily of resin acids, a class of tricyclic carboxylic acids, but also contains minor amounts of dimerized rosin and unsaponifiable matter. Because of the complex nature of their composition, rosin and the rest of the compounds in this group are considered to be "Class 2" substances.

Rosin is an important commercial material and has been used for centuries. Industrially, there are three different types of rosin: gum, wood and tall oil rosin, with the name indicating the way in which the rosin is extracted from the tree. In the United States, tall oil rosin is by far the most commercially important variety. Rosin (CAS# 8050-09-7) also now includes CAS# 8052-10-6, rosin, tall oil, which was used in the 1990 IUR reporting on which the HPV program was based, pursuant to EPA's letter to PCA of March 13, 1992.

Rosin is used primarily as the raw material for the production of rosin derivatives, which go into the production of a wide variety of industrial products. For example, the largest use of rosin is in the production of derivatives for printing inks, adhesives, and coatings. Rosin salts are widely used in paper sizing. Other members of the group are used to produce soaps and detergents or to impart enhanced stability to specialty rosin-based adhesives.

Existing data on rosin and hydrogenated rosin already exist. Both rosin and hydrogenated rosin are non-toxic in acute toxicity tests in multiple species. Existing data from repeat-dose studies, including long-term carcinogenicity studies on both of these compounds, show low toxicity and no potential carcinogenic or reproductive effects.

Where applicable, PCA will conduct physical/chemical property and environmental fate testing on five of the substances in the group. (Two of the substances, rosin distillation overheads and rosin low boiling fraction, are nearly identical so that physical/chemical

testing will only be conducted on one of them.) PCA has elected to treat this group of chemicals as a category for purposes of the HPV program. Therefore, a representative of the category will be used for ecotoxicity and developmental toxicity testing (the additional tests needed to complete the SIDS endpoints).

Rosin (CAS# 8050-09-7) has been selected as the representative substance in this category for testing for the additional SIDS data. Rosin represents by far the greatest production volume, with almost four times more rosin manufactured than all other substances in this category combined. In addition, rosin is the raw material from which all the other category members are derived. Consequently, test results obtained on rosin will be most representative of the category.

PCA has reviewed existing data on these compounds. Available data demonstrate that both rosin and hydrogenated rosin have low toxicity following acute oral exposure. A number of repeat dose and long-term carcinogenicity studies also show low toxicity and no evidence of carcinogenicity for both rosin and hydrogenated rosin. Because neither rosin nor hydrogenated rosin were carcinogenic in long-term feeding studies, it is reasonable to conclude that neither of these substances is genotoxic. The sub-chronic studies demonstrating a lack of any toxicity to the reproductive organs fulfill the SIDS endpoint for reproductive toxicity. Because there are no data on developmental toxicity, rosin will be tested to fulfill this endpoint.

A brief summary of the available data for the substances in this category, and the anticipated additional testing, is described below in Table 1.

Table 1
Matrix of Available Adequate Data and Proposed Testing
On Rosins and Rosin Salts*

Chemical and CAS #	**Required SIDS Endpoints**										
	Partition Coef.	**Water Sol.**	**Biodeg.**	**Acute Fish**	**Acute Daph.**	**Acute Algae**	**Acute oral**	**Repeat Dose**	**In vitro genotox (bact.)**	**In vitro genotox (non-bact)**	**Repro/ Develop**
8050-09-7 Rosin	Test	Test	Adeq.	Test	Test	Test	Adeq.	Adeq.	Adeq.	Adeq.	Adeq. Repro/ Test Develop.
65997-06-0, Rosin, hydrogenated	Test	Test	Test	C	C	C	Adeq.	Adeq.	Adeq.	Adeq.	C
68425-08-1, Rosin, distillation overheads	Test	Test	Test	C	C	C	C	C	C	C	C
68783-82-4 Rosin, low boiling fraction	No test	No test	No test	C	C	C	C	C	C	C	C
61790-50-9, Rosin, potassium salt	Test	Test	Test	C	C	C	C	C	C	C	C
61790-51-0, Rosin, sodium salt	Test	Test	Adeq.	C	C	C	C	C	C	C	C

Adeq. Indicates adequate existing data
Test Indicates proposed testing
No test See test plan; essentially identical to rosin, distillation overheads.
C Indicates category read-down from existing or proposed test data on rosin.
***** No testing will be conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation and transport and distribution between environmental compartments as explained in the test plan.

Physical/Chemical Properties

Physical and chemical properties will be determined when appropriate. However, many of the physical and chemical properties are either inappropriate or cannot be measured for these compounds:

- Melting points will not be determined because these substances are complex mixtures and either will not give a sharp melting point when heated or will decompose before they melt.

- Boiling points cannot be determined because these substances are complex mixtures and will decompose before they boil.
- Vapor pressure of these chemicals under ambient conditions is essentially zero and experimental measurement is not possible.
- Water solubility of five of the compounds in this category will be determined.
- Partition coefficients will be tested for five of the substances for which data do not already exist. The partition coefficient testing likely will yield a range of values representing the various components, rather than a single value representing the mixture.

Environmental Fate

With respect to the SIDS environmental fate endpoints:

- Biodegradation data will be generated for three of the compounds for which data are not already available.
- Hydrolysis in water will not be determined for any of the compounds in this category because the members of this category lack a functional group that would be susceptible to hydrolysis.
- Photodegradation is not relevant, since the vapor pressure of these compounds is essentially zero and they could not enter the atmosphere.
- Transport and distribution between environmental compartments will not be determined due to the inability to provide usable inputs to the required model.

Ecotoxicity

- Existing ecotoxicity data are not reliable due to inconsistencies in, or artificial methods of, sample preparation. Consequently, using rosin, acute toxicity to fish, daphnia and algae will be retested under conditions that maximize solubility, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects.

Mammalian Toxicity

- For the SIDS human health endpoints, there are adequate data on acute toxicity, repeat dose toxicity, and reproductive effects for both rosin and hydrogenated rosin. Rosin and hydrogenated rosin have been shown to be non-toxic in these tests.
- The availability of two-year feeding studies on rosin and hydrogenated rosin showing a lack of carcinogenicity obviates the need for *in vitro* genotoxicity testing.
- A developmental toxicity study on rosin will be undertaken to fulfill this SIDS endpoint.

The Pine Chemicals Association, Inc. HPV Task Force includes the following companies:

Akzo Nobel Resins
Akzo Nobel - Eka Chemicals Incorporated
Arizona Chemical Company
Asphalt Emulsion Manufacturers Association
Boise Cascade Corporation
Cognis Corporation
Eastman Chemical Co. (including the former Hercules Inc. Resins Division)
Georgia-Pacific Resins Inc.
ICI Americas (including the former Uniqema)
Inland Paperboard & Packaging, Inc.
International Paper Co. (including the former Champion International Corporation)
Koch Materials Co.
McConnaughay Technologies, Inc.
Mead Corp.
Packaging Corporation of America
Plasmine Technology, Inc.
Raisio Chemicals
Rayonier
Riverwood International
Smurfit – Stone Container Corporation
Westvaco
Weyerhaeuser Co.

The Task Force will be filing multiple test plans covering various chemicals. Not all members of the Task Force produce the substances covered by this test plan.

I. Description of Rosins and Rosin Salts

The Pine Chemicals Association, Inc. (PCA) is sponsoring six HPV chemicals known collectively as Rosins and Rosin Salts. This category of chemicals consists of the following:

8050-09-7, Rosin
65997-06-0, Rosin, hydrogenated
68425-08-1, Rosin, distillation overheads
68783-82-4, Rosin, low boiling fraction
61790-50-9, Rosin, potassium salt
61790-51-0, Rosin, sodium salt

All of the members of this group are derived from rosin, which is a naturally occurring substance found in trees, predominantly pine trees. Rosin is composed primarily of resin acids, a class of tricyclic carboxylic acids, but also contains minor amounts of dimerized rosin and unsaponifiable matter.   As complex mixtures, rosin and its derivatives are all considered as Class 2 substances.

Rosin is an important commercial material and has been used for centuries. Industrially, there are three different types of rosin: gum, wood and tall oil rosin, with the name indicating the way in which rosin is extracted from the tree. Gum rosin is obtained by slashing the tree and collecting the gummy exudates (oleoresin). This exudate consists of a mixture of rosin and turpentine and the rosin is recovered by distilling away the turpentine. Wood rosin is obtained by the solvent extraction of pine wood. Tall oil rosin is obtained by the distillation of tall oil, a by-product from the alkaline pulping of pine wood. In the United States, tall oil rosin is by far the most commercially important form of rosin.

The three rosins are chemically very similar. They all contain the same resin acids but the ratio of the acids is different. The difference arises because some of the resin acids are thermally unstable and isomerize to other resin acids during the production process. In 1991, the Pine Chemicals Association (then the Pulp Chemicals Association) proposed to the EPA that there should only be one CAS registry number to describe all three types of rosin. In a letter dated March 13, 1992, the Inventory Section of the EPA agreed with this request stating, *"… rosin, CASRN 8050-09-7 will cover all types of rosin, irrespective of their method of production."*   Subsequently, the industry and the EPA have only used one CAS number for rosin.   Thus, CAS# 8050-09-7 now also includes substances formerly reported as CAS# 8052-10-6.

A. Composition

Each species of pine tree has a somewhat different mix of resin acids. Even within a species, the mix of resin acids may be influenced by the climate and local terrain. However, all the members of this group are derived from rosin. “Hydrogenated rosin,” as the name implies, is made by the catalytic hydrogenation of rosin.   “Rosin, distillation overheads" is formed as a by-product when rosin is processed at high temperatures and is made up primarily of resin acids and decarboxylated resin acids. Rosin, low boiling fraction is essentially identical to rosin, distillation overheads. The sodium and potassium salts are simply rosin that has been reacted with the appropriate base.

The general characteristics and composition of each of the substances in this category are addressed below.

1. Rosin (CAS# 8050-09-7)

Rosin is a pale yellow, glass-like solid. The description of rosin listed in Appendix A of the TSCA Inventory is *"A complex combination derived from wood, especially pine wood. Composed primarily of resin acids and modified resin acids such as dimers and decarboxylated resin acids. Includes rosin stabilized by catalytic disproportionation."*

The composition of a typical tall oil rosin is shown in Table 2. As is evident, it consists of several major components and some minor ones. Rosin also contains trace quantities of numerous other components. Due to its complex composition, rosin is classified as a Class 2 substance. The structures of some of the more important resin acids found in rosin are shown in Figure 1.

Commercially, rosin is rarely categorized by its composition. Rather, it is usually specified by its softening point, acid value, and color (Zinkel and Russell 1989). In fact, the Naval Stores Act of 1923 (7 USC §§ 91-99), as amended in 1951, and regulations promulgated thereafter by USDA list only color as a specification for rosin.

Table 2

Composition of a Typical Tall Oil Rosin

Resin acid	Composition
Pimaric	4%
Sandarcopimaric	4%
Communic	1%
Palustric	8%
Isopimaric	11%
Abietic	38%
Dehydroabietic	18%
Neoabietic	3%
Other compounds[a]	12%

a: other resin acids, high boiling fatty acids and unsaponifiable matter.

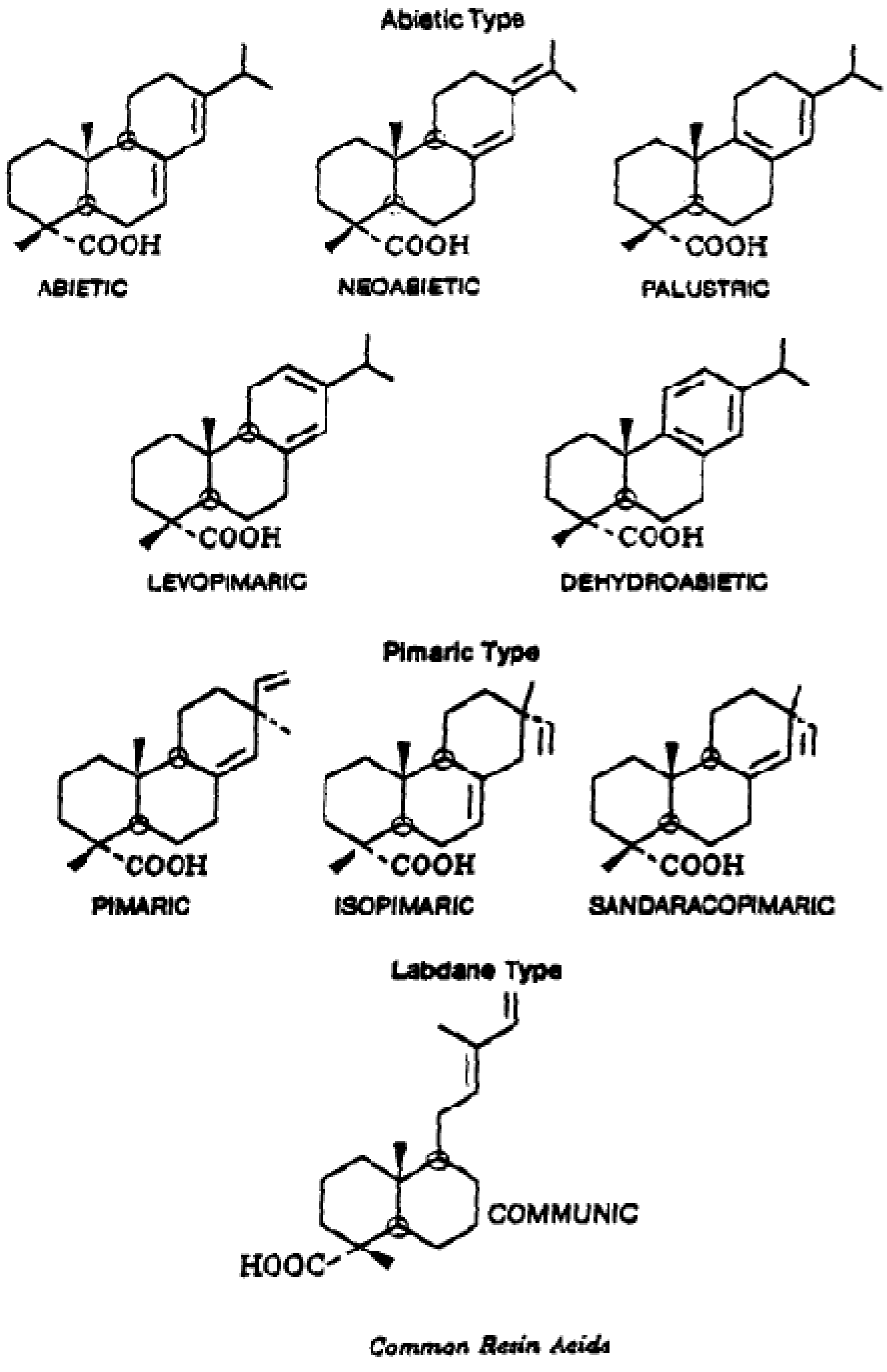

Figure 1. Representative resin acids found in rosin and its derivatives.

2. Rosin, hydrogenated (CAS# 65997-06-0)

The composition of hydrogenated rosin is similar to rosin except that some of the double bonds in the resin acids have been removed. The conjugated double bonds in resin acids such as abietic acid are prone to oxidation and so catalytic hydrogenation is used to stabilize the molecule. The resulting product retains its color and other oxidation sensitive properties better than unmodified rosin. Like rosin, hydrogenated rosin is characterized primarily by its color, softening point stability and acid value rather than its chemical composition.

3. Rosin, Distillation Overheads (CAS# 68425-08-1) and Rosin, Low Boiling Fraction (CAS# 68783-82-4)

Rosin, distillation overheads, is one of several substances listed in the inventory that describe the product obtained when rosin is heated to the temperature at which it degrades. Another, virtually identical, substance is rosin, low boiling fraction. Descriptions of both these substances are listed in Appendix A of the TSCA Inventory and the descriptions of each are essentially the same. Rosin, distillation overheads, is described *as "the low boiling fraction obtained by the distillation of rosin. Contains decarboxylated rosin, decarboxylated resin acids, resin acids, terpenes and hydrocarbons derived from decarboxylated fatty acids."* Rosin, low boiling fraction is described as *"A complex combination obtained by the distillation of rosin. This low boiling fraction consists primarily of decarboxylated rosin, resin acids, decarboxylated resin acids, terpenes and hydrocarbons derived from decarboxylated fatty acids."*

Based on this similarity, testing for chemical/physical properties will only be conducted on rosin, distillation overheads and no testing will be done on the rosin, low boiling fraction. As these substances are by-products of other processes the composition can vary widely as shown in Table 3.

Table 3

Composition of a Typical Rosin, Distillation Overheads

Fatty acids	1-5%
Rosin acids	30-60%
Hydrocarbons[a]	20-40%
Rosin aldehydes	10-20%
Rosin alcohols	5-10%
Rosin esters	1-10%

a: terpenic and from decarboxylated rosin acids and fatty acids

4. Rosin, Potassium Salt (CAS# 61790-50-9) and Sodium Salt (CAS# 61790-51-0)

The rosin potassium and sodium salts are merely the simple alkali metal salts of unmodified rosin and are made by treating rosin with the appropriate base. As these substances are salts of a strong base and a weak acid they are alkaline with the pH depending on the concentration.

B. Commercial Uses of Rosins and Rosin Salts

Rosin is by far the most important member of this category from a commercial standpoint, with almost four times the volume of production as the other members of the group combined. The main use of rosin is in the production of derivatives or chemical intermediates that find a wide variety of industrial applications. The largest single application for rosin derivatives is in the production of printing inks, followed by adhesive, chewing gum, and coatings.

Salts of rosin are widely used in the paper and the soap and detergents industries. The sodium salts of rosin are used in paper sizing chemicals to give the finished product a better surface finish and water resistance. Potassium salts of rosin are used in the production of various soaps and detergents.

Rosin, hydrogenated is used in specialty adhesive applications where product stability and color are important. It is useful for these applications because it does not oxidize as readily as rosin.

Rosin, distillation overheads and rosin, low boiling fraction find application in the production of rosin derivatives for the end use applications described above, or if the quality of the substances is undesirable, they may be consumed for their fuel value.

C. Complexity of Analytical Methodology

All of the substances in this category are Class 2 substances. This, combined with the fact that rosin is essentially insoluble in water and decomposes on heating at high temperature, creates a variety of analytical challenges. Gas chromatography of methylated derivatives is the accepted method for the analysis of the members of this category. PCA has verified the reliability of the standard analytical methods at concentrations lower than the 10 ppm limit of solubility for these substances. Based on the method validation work to date, it appears that the analytical procedures will be adequate for the proposed testing.

II. Rationale for Selection of Representative Compound for Testing

Rosin (CAS# 8050-09-7) has been selected as the representative substance in this category for testing for the applicable SIDS ecotoxicity and developmental toxicity tests, as shown in Table 4 (identical to Table 1). As further indicated in Table 4, pertinent physical/chemical properties and environmental fate endpoints will be determined for all five members of this category where data are not already available.

Table 4
Matrix of Available Adequate Data and Proposed Testing
On Rosin and Rosin Salts*

Chemical and CAS #	**Required SIDS Endpoints**										
	Partition Coef.	**Water Sol.**	**Biodeg.**	**Acute Fish**	**Acute Daph.**	**Acute Algae**	**Acute oral**	**Repeat Dose**	**In vitro genotox (bact.)**	**In vitro genotox (non-bact)**	**Repro/ develop**
8050-09-7 Rosin	Test	Test	Adeq.	Test	Test	Test	Adeq.	Adeq.	Adeq.	Adeq.	Adeq Repro./ Test Develop.
65997-06-0, Rosin, hydrogenated	Test	Test	Test	C	C	C	Adeq.	Adeq.	Adeq.	Adeq.	C
68425-08-1, Rosin, distillation overheads	Test	Test	Test	C	C	C	C	C	C	C	C
68783-82-4 Rosin, low boiling fraction	No test	No test	No test	C	C	C	C	C	C	C	C
61790-50-9, Rosin, potassium salt	Test	Test	Test	C	C	C	C	C	C	C	C
61790-51-0, Rosin, sodium salt	Test	Test	Adeq.	C	C	C	C	C	C	C	C

Adeq. Indicates adequate existing data
Test Indicates proposed testing
NoTest See test plan; essentially identical to rosin, distillation overheads
C Indicates category read-down from existing or proposed test data on rosin.
***** No testing will be conducted for melting point, boiling point, vapor pressure, hydrolysis, photodegradation and transport and distribution between environmental compartments as explained in the test plan.

All the substances in this category are similar in chemical composition, being predominantly a mixture or resin acids or their salts. The selection of rosin as the substance to be tested is based on two factors. It has by far the greatest production volume. Production of rosin in the U.S. is almost four times higher than production of the other substances in this category combined. EPA guidance suggests that testing the substance produced at the greatest volume as the representative chemical of a category would be appropriate. Clearly, rosin fits this criterion. In addition, rosin is the raw material from which all the other category members are derived.

Another criterion listed by EPA for grouping chemicals into a category is the use of the "family approach" of examining related chemicals when they are acids or acid salts. Although the salts of rosin have quite different physical characteristics, they are included in this category because they are quickly converted into the free acids when they are neutralized by acid or by dilution, as they would be under typical toxicity testing conditions. In summary, this group of chemicals fits the requirements of the EPA's HPV Challenge program for a chemical category, and rosin is the most appropriate representative test material from this category.

III. Review of Existing Data and Development of Test Plan

PCA has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for the chemicals in this category. Considerable data are available that satisfy most of the SIDS endpoints for this category. The availability of the data on the specific SIDS endpoints is summarized in Table 4 (identical to Table 1). Table 4 also shows data gaps that will be filled by additional testing, and areas where data from rosin and hydrogenated rosin will be generalized to other category members.

A. Evaluation of Existing Physicochemical Data and Proposed Testing

The basic physicochemical data required in the SIDS battery includes melting point, boiling point, vapor pressure, partition coefficient (K_{ow}), and water solubility.

Class 2 substances are composed of a complex mixture of substances and are often difficult to characterize. Rosin and its derivatives are not only Class 2 substances, but also are derived from natural sources. Their composition is variable and cannot be represented by a single chemical structural diagram. Due to this “complex mixture” characteristic of rosin and related compounds, some physical property measurements, such as partition coefficient do not give singe definitive results because the methodology used to determine these properties will actually fractionate or partition the substance into various components. Since the methodology will alter the actual sample composition, the results are likely to be erroneous, difficult to interpret, or meaningless.

1. Melting Point

Due to their complex nature, none of the members of this category have a well-defined melting point. These substances soften when heated and so have softening points rather than a true melting point. The softening point of these compounds can cover a wide range depending on the levels of resin acids, decarboxylated rosin and dimerized rosin in the sample, and hence these substances do not have specific softening points. The salts of rosin decompose on heating, and so melting point has no significance for these materials. Consequently, the melting point of these substances will not be measured.

2. Boiling Point

All of the members of this category are produced by high temperature, high vacuum distillation and are non-volatile solids at ambient temperatures. A boiling point at ambient temperature has no significance because these materials will thermally decompose before they boil. Accordingly, measurement of this property is inappropriate for all the substances in this category.

3. Vapor Pressure

Vapor pressures for the rosins (which are solids) at ambient temperatures are effectively zero, and their experimental measurement is inappropriate. When rosin salts are dissolved in water, their solutions will reflect the vapor pressure of the water rather than the salt, and therefore measurement of this property is inappropriate.

4. Water Solubility

The water solubility of five of the compounds in this category will be determined using OECD (105).

5. Partition Coefficient

The partition coefficient (i.e., K_{ow}) for five compounds in this category will be determined. Adequate data exist for rosin although it will be retested with the other compounds in this category. For rosin, existing data demonstrate that a range of K_{ow} values, rather than a single value, are generated when this endpoint is determined. This outcome reflects the complex nature of Class 2 mixtures.

Summary of Physicochemical Properties Testing: The water solubility and partition coefficients of five of the substances in this category will be determined. Adequate data on partition coefficient exist for rosin although it will be retested with the other compounds in this category. Tests for melting point, boiling point, and vapor pressure are inapplicable to these substances.

B. Evaluation of Existing Environmental Fate Data and Proposed Testing

The fate or behavior of a chemical in the environment is determined by the reaction rates for the most important transformation (degradation) processes. The basic environmental fate data covered by the HPV Program include biodegradation, stability in water (hydrolysis as a function of pH), photodegradation and transport and distribution between environmental compartments.

1. Biodegradation

Biodegradability provides a measure for the potential of compounds to be degraded by microorganisms. Depending on the nature of the test material, several standard test methods are available to assess potential biodegradability.

Two of the chemicals in this category (rosin and the sodium salt of rosin) have existing data on the biodegradation endpoint. Biodegradation for hydrogenated rosin, rosin distillation overheads and the potassium salt will be determined using OECD method 302B for the salt and OECD method 301B for the non-salts.

2. Hydrolysis

Hydrolysis as a function of pH is used to assess the stability of a substance in water. Hydrolysis is a reaction in which a water molecule (or hydroxide ion) substitutes for another atom or group of atoms present in an organic molecule. If there is no functional group suitable to be displaced, then the organic compound is considered to be resistant to hydrolysis. None of the substances in the rosin category contains an organic functional group that might be susceptible to this physical degradative mechanism. Therefore, hydrolysis need not be measured.

In addition, low water solubility often limits the ability to determine hydrolysis as a function of pH. All of the non-salt rosin compounds have very low solubility in water. Therefore, these materials are expected to be stable in water and it would be unnecessary to attempt to measure the products of hydrolysis. With respect to the rosin salts, in an aqueous medium they hydrolyze (ionize) immediately, but form stable species. Consequently, it would also be unnecessary to measure this endpoint for the rosin salts.

3. Photodegradation

Due to their lack of any vapor pressure under ambient conditions, there is essentially no opportunity for any of these chemicals to enter the atmosphere. Thus, photodegradation is irrelevant. In addition, based on the constituents in these complex mixtures, there is no reason to suspect that they would be subject to breakdown by a photodegradative mechanism. Consequently, this endpoint will not be determined for any of the substances in this category.

4. Transport and Distribution Between Environmental Compartments

The transport and distribution between environmental compartments is intended to determine the ability of a chemical to move or partition in the environment. The determination of this property requires the use of various models (e.g., level III model from the Canadian Environment Modeling Centre at Trent University). For Class 2 substances such as rosin and related compounds, the required inputs to the model are either not available or impossible to determine including molecular mass, reaction halflife estimates for air, water, soil, sediment, aerosols, suspended sediment, and aquatic biota. In addition, while the partition coefficient is also required and can be determined, the multiple K_{ow} values typically derived for these substances (e.g., five K_{ow} values for rosin) are a consequence of sample fractionation and reflect various components in the

transportation and distribution between environmental compartments will be undertaken for rosin and related compounds.

Summary of Environmental Fate Testing: Biodegradation data will be generated for three of the compounds in this category for which data are not already available using OECD method 302B for the salt and OECD method 301B for the non-salts. Photodegradation, hydrolysis and transport and distribution between environmental compartments are not applicable to these chemicals.

C. Evaluation of Existing Ecotoxicity Data and Proposed Testing

The basic ecotoxicity data that are part of the HPV Program include acute toxicity to fish, daphnia and algae. While there are existing data on these endpoints for some of the substances in this grouping category, these data are conflicting and it is impossible to determine which, if any, of these findings is representative of true ecotoxicity. The inconsistencies in how water samples were prepared for testing these endpoints render these data inadequate. Consequently, acute toxicity to fish, daphnia and alga will be retested for rosin under conditions that maximize the solubility under the specific test exposure conditions, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects. In addition, the effect of both filtering, to further minimize nonspecific physical effects, and of reducing the pH to the lower end of the acceptable range for test organism survival, will also be investigated for changes in toxicological effects. The results of preliminary tests will be used to select the most appropriate test conditions for the definitive test for each species.

Summary of Ecotoxicity Testing: The acute toxicity of rosin to fish, daphnia and algae will be tested under conditions that maximize solubility, but reduce exposure to insoluble fractions, which may cause nonspecific toxicological effects.

D. Evaluation of Existing Human Health Effects Data and Proposed Testing

1. Acute Oral Toxicity

Acute oral toxicity studies investigate the effect(s) of a single exposure to a relatively high dose of a substance. This test is conducted by administering the test material to animals (typically rats or mice) in a single gavage dose. Harmonized EPA testing guidelines (August 1998) set the limit dose for acute oral toxicity studies at 2000 mg/kg body weight. If less than 50 percent mortality is observed at the limit dose, no further testing is needed.   A test substance that shows no effects at the limit dose is considered essentially nontoxic. If compound-related mortality is observed, then further testing may be necessary.

Summary of Available Acute Oral Toxicity Data

Both rosin and hydrogenated rosin are non-toxic following acute oral exposure. The acute oral LD_{50} values of various rosins (wood, gum and tall oil) are > 4000 mg/kg in rats, mice and guinea pigs. The acute oral LD_{50} value of hydrogenated rosin is > 32,000 mg/kg.

Summary of Acute Oral Toxicity Testing: Both rosin and hydrogenated rosin have been tested for acute oral toxicity and found to be non-toxic (i.e., LD_{50} > 4000 mg/kg) well above the guideline of 2000 mg/kg. Consequently, additional testing for this endpoint is not necessary.

2. Repeat Dose Toxicity

Subchronic repeat dose toxicity studies are designed to evaluate the effect of repeated exposure to a chemical over a significant period of the life span of an animal. Typically, the exposure regimen in a subchronic study involves daily exposure (at least 5 consecutive days per week) for a period of not less than 28 days or up to 90 days (i.e., 4 to 13 weeks). The HPV program calls for a repeat dose test of at least 28 days. The dose levels evaluated are lower than the relatively high doses used in acute toxicity (i.e., LD_{50}) studies. In general, repeat dose studies are designed to assess systemic toxicity, but the study protocol can be modified to incorporate evaluation of potential adverse reproductive and/or developmental effects.

Summary of Available Repeat Dose Toxicity Data

There are existing data that demonstrate low toxicity for both rosin and hydrogenated rosin in repeat dose tests. Rosin was tested in a 90-day subchronic toxicity study in rats. The test material was administered to Sprague-Dawley rats in the diet at concentrations of 0, 0.01, 0.05, 0.20, 1.0 and 5.0% for 90 days. The approximate doses were 0, 10, 50, 200, 1000, or 5000 mg/kg/day. Parameters evaluated included clinical signs, mortality, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, gross and microscopic pathology, and organ weights.

All animals in the 5% dose group died within a week due to palatability issues resulting in complete cessation of food consumption. Some animals in the 1% dose group also failed to gain weight compared to controls due to decreased food consumption that resulted in some decreased organ weight to body weight ratios. No changes in hematology, clinical chemistry or urinalysis parameters were measured at any dose level. At gross pathology, no treatment-related effects were noted. No consistent organ weight changes and no histopathological effects were reported. Based on these data, the No Observed Effect Level (NOEL) was 0.20% (approximately 200 mg/kg/day).

Other 90-day subchronic studies confirm the low toxicity of rosin. In these studies, the only effect noted was either death due to palatability resulting in non-consumption of food or depression of body weight gain at the highest doses tested. In a dietary study with hydrogenated rosin, weanling Sprague-Dawley rats were exposed at concentrations of 0, 0.01, 0.05, 0.2, 1, or 5% for 90 days. The approximate doses were 0, 10, 50, 200, 1000, or 5000 mg/kg/day. Parameters evaluated included clinical signs, mortality, body weight, body weight gain, food utilization, hematology parameters, urinalysis, organ weights and gross and microscopic pathology.

All the animals in the high-dose group died prior to study termination due to treatment-related starvation through food refusal. In the 1% group, body weight was significantly decreased in both males and females, and food consumption was decreased. Food utilization was not affected at a dietary concentration of 1% indicating that the reduced food consumption was related to palatability. No treatment-related effects on hematology, urinalysis, or gross or microscopic pathology. Based on these data, the NOEL was 0.2% (approximately 200 mg/kg/day).

Summary of Repeat Dose Toxicity Testing: Rosin and hydrogenated rosin have been tested for repeat dose toxicity in 90-day studies. In these studies, the NOELs for both rosin and hydrogenated rosin were approximately 200 mg/kg/day, indicating that these compounds have low toxicity. Additional studies on these compounds support this result. Consequently, no additional testing for this endpoint will be conducted.

3. Genotoxicity – In vitro

Genetic testing is conducted to determine the effects of substances on genetic material (i.e., DNA and chromosomes). The gene, which is composed of DNA, is the simplest functional genetic unit. Mutations of genes can occur spontaneously or as a consequence of exposure to chemicals or radiation. Genetic mutations are commonly measured in bacterial and mammalian cells, and the HPV program calls for completing both types of tests.

Summary of Available Genotoxicity Data

Rosin and hydrogenated rosin have been tested for potential carcinogenicity in several two-year bioassays conducted in rats. None of these studies demonstrated any evidence of carcinogenicity. The primary effect was depressed weight gain at the highest dose, confirming that a maximally tolerated dose was achieved.

Since the purpose of *in vitro* bacterial and mammalian mutagenicity tests is to determine if a chemical might have the potential to be a direct-acting DNA reactive carcinogen, the negative carcinogenicity studies eliminate the need to test for potential genotoxicity.

Summary of Genotoxicity Testing: Neither rosin nor hydrogenated rosin were carcinogenic when tested in two-year cancer bioassays. Consequently, no genotoxicity testing is necessary.

4. Reproductive and Developmental Toxicity

Reproductive toxicity includes any adverse effect on fertility and reproduction, including effects on gonadal function, mating behavior, conception, and parturition. Developmental toxicity is any adverse effect induced during the period of fetal development, including structural abnormalities, altered growth and post-partum development of the offspring.

The “toxicity to reproduction” aspect of the HPV Challenge Program can be met by conducting a reproductive/developmental toxicity screening test or adding a reproductive/developmental toxicity screening test to the repeat dose study (OECD 421 or OECD 422, respectively). The one-generation reproduction toxicity study (OECD 415) is a more comprehensive protocol for the study of the effect of a test material on reproduction and development that also meets the SIDS and the HPV Program requirements.

Summary of Reproductive/Developmental Toxicity Data

As noted in the SIDS guidelines for the reproduction toxicity endpoint, *"when a 90-day repeated dose study is available and demonstrates no effects on the reproductive organs, in particular the testes, then a developmental study can be considered as an adequate test to complete information on reproduction/developmental effect."* Rosin and hydrogenated rosin have been tested in 90-day repeat dose studies as well as in two-year bioassays. Both types of studies included histopathology of reproductive organs (*i.e.*, testes, ovaries, uterus) and showed no evidence of reproductive organ toxicity at any dose level. Therefore, these studies satisfy the SIDS reproductive toxicity endpoint. However, since neither of these studies evaluated the developmental toxicity endpoint, this will be determined on rosin using OECD protocol 421.

Summary of Reproductive/Developmental Testing: Neither rosin nor hydrogenated rosin demonstrated any effects on reproductive toxicity in numerous repeat dose studies. However, since none of these studies evaluated potential developmental toxicity, rosin will be tested for this endpoint with OECD protocol 421.

References

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